HYPONATREMIA PART 2

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TREATMENT

- Because the brain cannot swell by much more than 5%, correction of hyponatremia by this amount would be expected to prevent the most serious complications of acute water intoxication; empirical observations support this prediction.

- An increase in the plasma sodium concentration of 4 to 6 mmol per liter is enough to reverse impending brain herniation or stop active seizures in patients with severe acute hyponatremia.

- Such an increase can be reliably achieved with 100-ml bolus infusions of 3% saline (2 ml per kilogram in small patients), administered at 10-minute intervals to a total of three doses, if necessary, to control symptoms.

Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. Semin Nephrol 2009; 29: 282-99.

- Milder symptoms of acute hyponatremia should be treated with enough 3% saline to avoid a worsening of hyponatremia because of delayed absorption of ingested water or excretion of hypertonic urine.

Bhaskar E, Kumar B, Ramalakshmi S. Evaluation of a protocol for hypertonic saline administration in acute euvolemic symptomatic hyponatremia: a prospective observational trial. Indian J Crit Care Med 2010; 14: 170-4.

Treatment and Limits of Correction of Severe Hyponatremia.*

Duration	Related Behavior or Condition	Clinical Features	Initial Therapeutic Goal	Limit of Correction and Management of Overcorrection
Several hours	Self-induced water intoxication associated with psychosis, running in marathons, use of 3,4-methylenedioxymethamphetamine (MDMA, or "ecstasy")	Headache, delirium, vomiting, seizures, coma, neurogenic pulmonary edema, brain swelling with risk of fatal herniation	100-ml bolus of 3% saline three times as needed for severe symptoms; increase plasma sodium concentration by 4–6 mmol/liter in first 6 hr	Excessive correction not known to be harmful
1–2 days	Postoperative hyponatremia, especially in women and children; hyponatremia associated with intracranial disease	Headache, delirium, vomiting, seizures, coma, neurogenic pulmonary edema, brain swelling with risk of fatal herniation	100-ml bolus of 3% saline three times as needed for severe symptoms; increase plasma sodium concentration by 4–6 mmol/liter in first 6 hr	Avoid increasing plasma sodium concentration by >10 mmol/liter/day
Unknown or ≥2 days	Conditions associated with high risk of the osmotic demyelination syndrome (plasma sodium concentration, 105 mmol/liter or less; hypokalemia, alcoholism, malnutrition, liver disease)†	Malaise, fatigue, confusion, cramps, falls, 10% incidence of seizures with plasma sodium concentration <110 mmol/liter, minimal brain swelling, and no risk of herniation	Extra caution indicated for conditions associated with high risk of osmotic demyelination syndrome; 100- ml bolus of 3% saline if needed for seizures; increase plasma sodium concentration by 4–6 mmol/liter in first 24 hr	Avoid increasing plasma sodium concentration by >8 mmol/liter/day; consider lowering again if limit is exceeded, especially in patients with high risk of the osmotic demyelination syndrome

* Severe hyponatremia is defined as a plasma sodium concentration below 120 mmol per liter. In the absence of urinary loss of water, 1 ml of 3% saline per kilogram of body weight will increase the plasma sodium concentration by approximately 1 mmol per liter.

† The osmotic demyelination syndrome may develop when the plasma sodium concentration is increased rapidly in outpatients who became hyponatremic while drinking normal amounts of water and in hospitalized patients who became hyponatremic over 2 or more days.

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- Hyponatremia is usually a chronic condition and it should be presumed to be chronic when the actual duration is unclear.

- To reduce symptoms and improve potential outcomes, chronic hyponatremia should be corrected gradually with the use of fluid restriction, salt tablets, slow infusions of 3% saline, furosemide, demeclocycline, urea, or vasopressin antagonists, or by treatment of the underlying cause.

ROLE OF VAPTANS

- AVP antagonists (vaptans) are highly effective in SIAD and in hypervolemic hyponatremia due to heart failure or cirrhosis, reliably ↑ing plasma Na^+ concentration due to their “aquaretic” effects .

- Tolvaptan is currently the only oral V2 antagonist to be approved by the U.S. FDA. Conivaptan, the only available intravenous vaptan, is a mixed V1A/V2 antagonist, with a modest risk of hypotension due to V1A receptor inhibition. Therapy with vaptans must be initiated in a hospital setting, with a liberalization of fluid restriction (>2 L/d).

- Repeat therapeutic lowering of the plasma sodium concentration is justified if the correction of hyponatremia exceeds 8 mmol per liter per day and there are risk factors for osmotic demyelination or if the correction is 10 to 12 mmol per liter per day without these risk factors.

Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 2013; 126: Suppl 1: S1-S42.

- To prevent inadvertent overcorrection, desmopressin can be administered preemptively, in anticipation of, rather than in response to, unwelcome urinary losses of water; hyponatremia is corrected with a slow infusion of 3% saline while the urine is kept concentrated with repeated doses of desmopressin.

Sood L, Sterns RH, Hix JK, Silver SM, Chen L. Hypertonic saline and desmopressin: a simple strategy for safe correction of severe hyponatremia. Am J Kidney Dis 2013; 61: 571-8.

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- The traditional approach is to calculate an Na+ deficit, where the Na deficit = 0.6 × body weight × (target plasma Na concentration – starting plasma Na+ concentration), followed by a calculation of the required rate.

- **Water restriction:** The amount of fluid restriction necessary depends on the extent of water elimination. A useful guide to the necessary degree of fluid restriction is as follows:
  - If (Urine Na + Urine K)/Serum Na+ is < 0.5, restrict to 1 L/d.
  - If (Urine Na + Urine K1)/Serum Na+ is 0.5 to 1.0, restrict to 500 mL/d.
  - If (Urine Na+Urine K)/Serum Na+ is >1, the patient has a negative renal free water clearance and is actively reabsorbing water.

- The most accurate way to correct hyponatremia entails a detailed registry matching total solute and water output with desired input. In clinical practice, this is often impractical.
- In lieu of this, the following equation is often used to approximate the change in $[Na^+]$ in mEq/L from the infusion of 1 L of fluid:

$$\Delta[\mathbf{Na}^+] = \{[\mathbf{Na}^+_i] + [\mathbf{K}^+_i] - [\mathbf{Na}^+_s]\} \div \{\mathbf{TBW} + 1\}$$

  $[Na^+_i]$ and $[K^+_i]$ are the sodium and potassium concentrations in the infused fluid, and $[Na^+_s]$ is the starting serum sodium (*Intensive Care Med 1997;23:309*). Recall that TBW is estimated by multiplying the lean weight (in kilograms) by 0.6 in men (and 0.5 in women). This formula does not account for ongoing electrolyte or water losses and is only a rough guide.
- Dividing the desired rate of correction (mEq/L/hr) by $\Delta[Na^+]$ (mEq/L/L of fluid) gives you the appropriate **rate of administration (liter of fluid per hour)**.

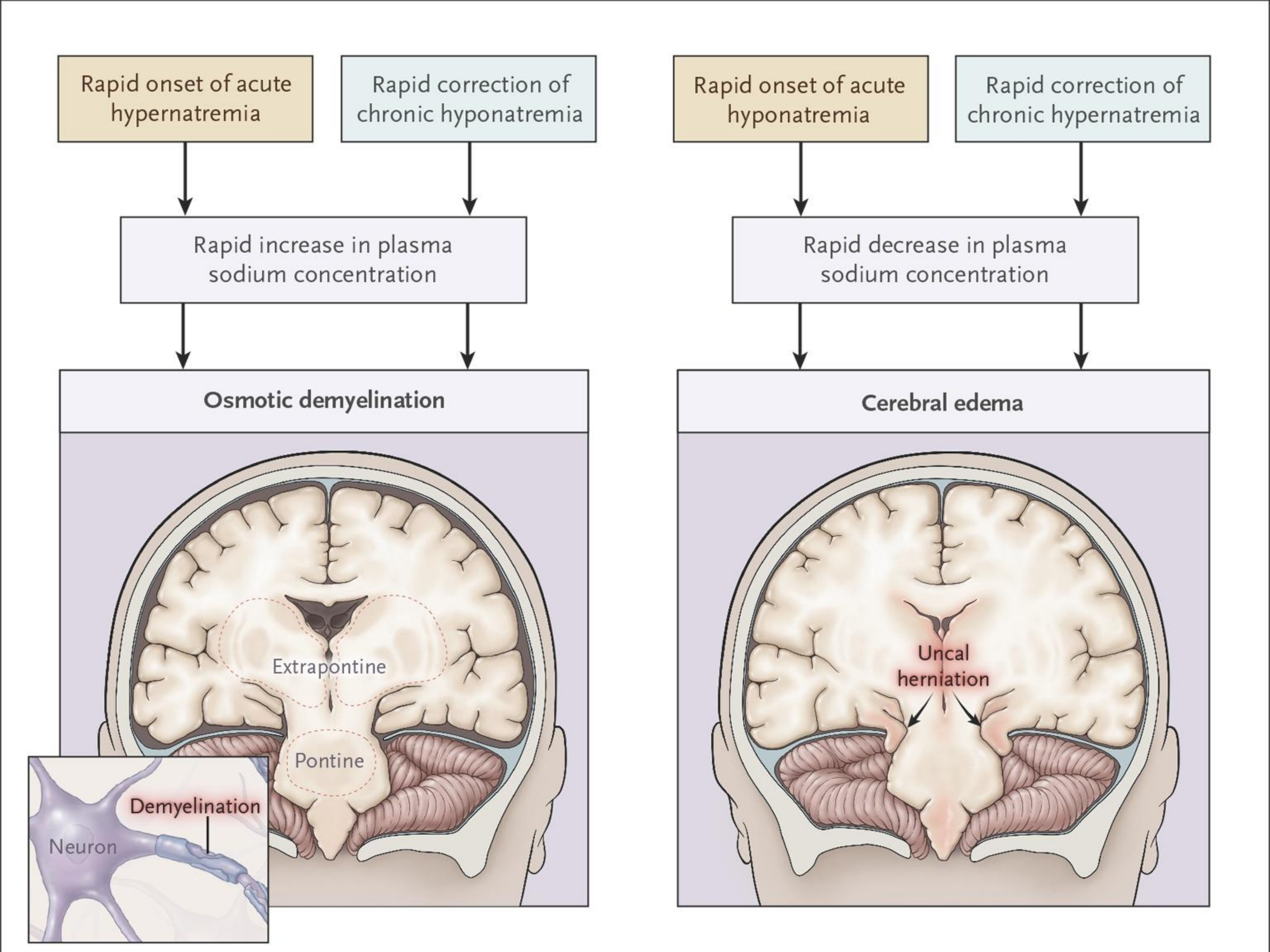
- **Example:** An 80-kg woman is seizing. Her $[Na^+]$ is 103 mEq/L.
  - **Rate of correction:** She has symptomatic hyponatremia requiring an acute correction (1 to 2 mEq/L/hr for the first 3 to 4 hours) but no more than 12 mEq/L corrected over 24 hours.
  - **Means of correction:**
    - Given the acuity, the patient should be given hypertonic saline, which has 513 mEq of Na^+ per liter.
    - One liter of this fluid would increase $[Na^+]$ by 10 mEq/L.

$$\Delta[Na^+] = \{513 - 108\} \div \{80 \times 0.5 + 1\} = 10 \text{ mEq/L}$$

    - Dose hypertonic saline at 200 mL/hr until symptoms improve.

$$\text{Rate} = [2 \text{ mEq/L/hr}] \div [10 \text{ mEq/L per 1 L of saline}]$$

  - To prevent a change of >10 to 12 mEq/L over 24 hours, no more than 1 L of fluid should be given.



Rapid onset of acute hypernatremia
Rapid correction of chronic hyponatremia
Rapid increase in plasma sodium concentration
Osmotic demyelination
Extrapontine
Pontine
Demyelination
Neuron
Rapid onset of acute hyponatremia
Rapid correction of chronic hypernatremia
Rapid decrease in plasma sodium concentration
Cerebral edema
Uncal herniation

THANK YOU